

## REMARKS

In the Office Action mailed July 2, 2002, the Examiner restricted the 46 pending claims in the captioned application. The Examiner has required the Applicants to make an election of species. The Examiner indicates that the claims are directed to six patentably distinct species. Applicants hereby elect ✓ "a compound capable of stimulating an endogenous immune response" for prosecution in the captioned application. The claims readable on the elected species are amended claims 1-38 and 41-46 and new claim 47.

Claims 1 and 39-42 have been amended to delete the phrase "known to be." Claim 1 has been amended to replace the phrase "a ligand-immunogen conjugate composition comprising a complex of the ligand and an immunogen" with the phrase "a composition comprising an immunogen conjugated to the ligand." This claim amendment was made to point out more particularly that the phrase "a ligand-immunogen conjugate" in original claim 1 did not refer to a different ligand than the ligand that binds to the "accessible binding site for a ligand" as recited in the preamble of claim 1. The above-described claim amendments are similar to claim amendments made during International Stage Preliminary Examination of the counterpart PCT application. Claims 1, 22-26, 38, 41-43, and 45-46 have been amended in line with Applicants' response/election. Support for these claim amendments is found throughout the specification and in the claims as originally filed.

Respectfully submitted,



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1. (Amended) A method of enhancing an endogenous immune response-mediated specific elimination of a population of pathogenic cells in a host animal harboring said population wherein the members of said cell population have an accessible binding site for a ligand, said method comprising the step of  
  
administering to said host a [ligand-immunogen conjugate] composition comprising an immunogen conjugated to the ligand [a complex of the ligand and an immunogen] wherein said immunogen is [known to be] recognized by an endogenous or an exogenous antibody in the host or is [known to be] recognized directly by an immune cell in the host; and  
  
administering to said host [at least one additional composition comprising a therapeutic factor, said factor being selected from the group consisting of a cell killing agent, a tumor penetration enhancer, a chemotherapeutic agent, an antimicrobial agent, a cytotoxic immune cell, and] a compound capable of stimulating an endogenous immune response wherein the compound does not bind to the ligand-immunogen conjugate.
22. (Amended) The method of claim 1 wherein the compound capable of stimulating an endogenous immune response [therapeutic factor] comprises a cytokine.
23. (Amended) The method of claim 21 wherein the cytokine [therapeutic factor] comprises IL-2, IL-12, IL-15, or combinations thereof.
24. (Amended) The method of claim 21 wherein the cytokine [therapeutic factor] comprises IL-2, IL-12, IL-15, or combinations thereof, in combination with IFN- $\alpha$  or IFN- $\gamma$ .

having a glutamyl group wherein the covalent linkage to the immunogen is only through the  $\gamma$ -carboxy group of the glutamyl group.

40. (Amended) A method of enhancing an endogenous immune response-mediated specific elimination of a population of pathogenic cells in a host animal harboring said population wherein said population preferentially expresses, uniquely expresses, or overexpresses a binding site for a folic acid receptor, said method comprising the step of

administering to said host a composition comprising a covalently linked conjugate of an immunogen wherein the immunogen is [known to be] recognized by an endogenous or exogenous antibody in the host or is [known to be] recognized directly by an immune cell in the host[;] and a ligand comprising folic acid or a folic acid analogue having a glutamyl group wherein the covalent linkage to the immunogen is only through the  $\alpha$ -carboxy group of the glutamyl group.

41. (Amended) A method of enhancing an endogenous immune response-mediated specific elimination of a population of pathogenic cells in a host animal harboring said population wherein said population preferentially expresses, uniquely expresses, or overexpresses a binding site for a folic acid receptor, said method comprising the steps of

administering to said host a composition comprising a covalently linked conjugate of an immunogen wherein the immunogen is [known to be] recognized by an endogenous or exogenous antibody in the host or is [known to be] recognized directly by an immune cell in the host;

administering to said host a ligand comprising folic acid or a folic acid analogue having a glutamyl group wherein the covalent linkage is only through the  $\gamma$ -carboxy group of the glutamyl group; and

25. (Amended) The method of claim 21 wherein the cytokine [therapeutic factor] comprises IL-2, IL-12, IL-15, or combinations thereof, in combination with IFN- $\alpha$  or IFN- $\gamma$ , or a combination thereof, and GM-CSF.

26. (Amended) The method of claim 21 wherein the compound capable of stimulating an endogenous immune response [therapeutic factor] comprises at least one NK cell or T cell stimulant.

38. (Amended) A method of enhancing an endogenous immune response-mediated specific elimination of a population of pathogenic cells in a host animal harboring said population wherein said population expresses a binding site for a ligand, said method comprising the steps of

administering to the host a composition comprising a complex of said ligand and an immunogen;

administering to the host antibodies directed against the immunogen; and

administering to said host [at least one additional therapeutic factor, said factor being selected from the group consisting of a cell killing agent, a tumor penetration enhancer, a chemotherapeutic agent, an antimicrobial agent, a cytotoxic immune cell, and] a stimulant of an endogenous immune response that does not bind to the ligand-immunogen complex.

39. (Amended) A method of enhancing an endogenous immune response-mediated specific elimination of a population of pathogenic cells in a host animal harboring said population wherein said population preferentially expresses, uniquely expresses, or overexpresses a folic acid receptor, said method comprising the step of

administering to said host a composition comprising a covalently linked conjugate of an immunogen wherein the immunogen is [known to be] recognized by an endogenous or exogenous antibody in the host or is [known to be] recognized directly by an immune cell in the host[;] and a ligand comprising folic acid or a folic acid analogue

administering to said host [at least one additional composition comprising a therapeutic factor, said factor being selected from the group consisting of a cell killing agent, a tumor penetration enhancer, a chemotherapeutic agent, an antimicrobial agent, a cytotoxic immune cell, and] a compound capable of stimulating an endogenous immune response wherein the compound does not bind to the ligand-immunogen conjugate.

42. (Amended) A method of enhancing an endogenous immune response-mediated specific elimination of a population of pathogenic cells in a host animal harboring said population wherein said population preferentially expresses, uniquely expresses, or overexpresses a folic acid receptor, said method comprising the step of administering to said host a composition comprising a covalently linked conjugate of an immunogen wherein the immunogen is [known to be] recognized by an endogenous or exogenous antibody in the host or is [known to be] recognized directly by an immune cell in the host;

administering to said host a ligand comprising folic acid or a folic acid analogue having a glutamyl group wherein the covalent linkage is only through the  $\alpha$ -carboxy group of the glutamyl group; and

administering to said host [at least one additional composition comprising a therapeutic factor, said factor being selected from the group consisting of a cell killing agent, a tumor penetration enhancer, a chemotherapeutic agent, an antimicrobial agent, a cytotoxic immune cell, and] a compound capable of stimulating an endogenous immune response wherein the compound does not bind to the ligand-immunogen conjugate.

43. (Amended) A pharmaceutical composition comprising therapeutically effective amounts of a ligand-immunogen conjugate capable of specific binding to a population of pathogenic cells in a host animal for specific elimination of said cells by an acquired or innate immune response, co-administered antibodies, or directly by an immune cell in the host, [a therapeutic factor selected from the group consisting of a cell killing agent,

a tumor penetration enhancer, a chemotherapeutic agent, an antimicrobial agent, and] a compound capable of stimulating an endogenous immune response wherein the compound does not bind to the ligand-immunogen conjugate, and a pharmaceutically acceptable carrier therefor.

45. (Amended) The pharmaceutical composition of claim 42 wherein the [therapeutic factor is an immune stimulant] compound capable of stimulating an endogenous immune response is a cytokine.

46. (Amended) The pharmaceutical composition of claim [44] 45 wherein the [immune stimulant] cytokine comprises a compound selected from the group consisting of IL-2, IL-12, IL-15, IFN- $\alpha$ , IFN- $\gamma$ , and GM-CSF, or combinations thereof.